

09/676 301  
JH#14

=> s angiogen?  
L1 72095 ANGIOGEN?

=> s angiostatin  
L2 1746 ANGIOSTATIN

=> s inhibit?  
L3 4584269 INHIBIT?

=> s l1 and l2 and l3

L4 1200 L1 AND L2 AND L3

=> s express?  
L5 3116179 EXPRESS?

=> s l1 and l2 and l3 and l5

L6 381 L1 AND L2 AND L3 AND L5

=> dup rem l6  
PROCESSING COMPLETED FOR L6  
L7 209 DUP REM L6 (172 DUPLICATES REMOVED)

=> s l7 and py<1998

1 FILES SEARCHED...  
3 FILES SEARCHED...  
4 FILES SEARCHED...  
L8 18 L7 AND PY<1998

=> d ibib abs 1-18

L8 ANSWER 1 OF 18 BIOSIS COPYRIGHT 2002 BIOLOGICAL  
ABSTRACTS INC.  
ACCESSION NUMBER: 1997:448382 BIOSIS  
DOCUMENT NUMBER: PREV199799747585  
TITLE: Kringle 5 of plasminogen is a novel \*\*\*inhibitor\*\*\* of  
endothelial cell growth.  
AUTHOR(S): Cao, Yihai (1); Chen, Andrew; An, Seong Soo A.; Ji,  
Richard-Weidong; Davidson, Don; Cao, Yumei; Llinas, Miguel  
CORPORATE SOURCE: (1) Lab. Angiogenesis Res., Dep. Cell Mol. Biol.,  
Karolinska Inst., S-171 77 Stockholm Sweden  
SOURCE: Journal of Biological Chemistry, (1997) Vol. 272, No. 36,  
pp. 22924-22928.  
ISSN: 0021-9258.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
AB \*\*\*Angiostatin\*\*\* is a potent \*\*\*angiogenesis\*\*\* \*\*\*inhibitor\*\*\*

which has been identified as an internal fragment of plasminogen that  
includes its first four kringle modules. We have recently demonstrated  
that the anti-endothelial cell proliferative activity of  
\*\*\*angiostatin\*\*\* is also displayed by the first three kringle  
structures of plasminogen and marginally so by kringle 4 (Cao, Y., Ji,  
R.-W., Davidson, D., Schaller, J., Marti, D., Sohndel, S., McCance, S. G.,  
O'Reilly, M. S., Llinas, M., and Folkman, J. (1996) J. Biol. Chem. 271,  
29461-29467). We now report that the kringle 5 fragment of human  
plasminogen is a specific \*\*\*inhibitor\*\*\* for endothelial cell  
proliferation. Kringle 5 obtained as a proteolytic fragment of human  
plasminogen displays potent \*\*\*inhibitory\*\*\* effect on bovine  
capillary endothelial cells with a half-maximal concentration (ED-50) of  
approximately 50 nM. Thus, kringle 5 would appear to be more potent  
than

\*\*\*angiostatin\*\*\* on \*\*\*inhibition\*\*\* of basic fibroblast growth  
factor-stimulated capillary endothelial cell proliferation. Appropriately  
folded recombinant mouse kringle 5 protein, \*\*\*expressed\*\*\* in  
Escherichia coli, exhibits a comparable \*\*\*inhibitory\*\*\* effect as the  
proteolytic kringle 5 fragment. Thus, kringle 5 domain of human  
plasminogen is a novel endothelial \*\*\*inhibitor\*\*\* that is  
sufficiently potent to block the growth factor-stimulated endothelial cell  
growth.

L8 ANSWER 2 OF 18 BIOSIS COPYRIGHT 2002 BIOLOGICAL  
ABSTRACTS INC.  
ACCESSION NUMBER: 1996:539848 BIOSIS  
DOCUMENT NUMBER: PREV199699262204

TITLE: Human prostate carcinoma cells \*\*\*express\*\*\* enzymatic  
activity that converts human plasminogen to the  
\*\*\*angiogenesis\*\*\* \*\*\*inhibitor\*\*\*,  
\*\*\*angiostatin\*\*\*.

AUTHOR(S): Gately, Stephen; Twardowski, Przemyslaw; Stack, M.  
Sharon;

Patrick, Matthew; Boggio, Lisa; Cundiff, Deborah L.;  
Schnaper, H. William; Madison, Laird; Volpert, Olga; Bouck,  
Noel; Enghild, Jan; Kwaan, Hau C.; Soff, Gerald A. (1)

CORPORATE SOURCE: (1) Div. Hematol./Oncol., 303 E. Chicago Ave.,  
Searle

Build., Suite 3-565, Chicago, IL 60611 USA

SOURCE: Cancer Research, (1996) Vol. 56, No. 21, pp. 4887-4890.  
ISSN: 0008-5472.

DOCUMENT TYPE: Article

LANGUAGE: English

AB \*\*\*Angiostatin\*\*\* is an \*\*\*inhibitor\*\*\* of \*\*\*angiogenesis\*\*\*  
and metastatic growth that is found in tumor-bearing animals and can be  
generated in vitro by the proteolytic cleavage of plasminogen. The  
mechanism by which \*\*\*angiostatin\*\*\* is produced in vivo has not  
been  
defined. We now demonstrate that human prostate carcinoma cell lines  
(PC-3, DU-145, and LN-CaP) \*\*\*express\*\*\* enzymatic activity that  
can

generate bioactive \*\*\*angiostatin\*\*\* from purified human plasminogen  
or plasmin. Affinity purified PC-3-derived \*\*\*angiostatin\*\*\*  
\*\*\*inhibited\*\*\* human endothelial cell proliferation, basic fibroblast  
growth factor-induced migration, endothelial cell tube formation, and  
basic fibroblast growth factor-induced corneal \*\*\*angiogenesis\*\*\*.  
Studies with proteinase \*\*\*inhibitors\*\*\* demonstrated that a serine  
proteinase is necessary for \*\*\*angiostatin\*\*\* generation. These data  
indicate that bioactive \*\*\*angiostatin\*\*\* can be generated directly by  
human prostate cancer cells and that serine proteinase activity is  
necessary for \*\*\*angiostatin\*\*\* generation.

L8 ANSWER 3 OF 18 BIOSIS COPYRIGHT 2002 BIOLOGICAL  
ABSTRACTS INC.

ACCESSION NUMBER: 1995:433403 BIOSIS

DOCUMENT NUMBER: PREV199598447703

TITLE: \*\*\*Angiogenesis\*\*\* : Mechanistic insights, neovascular  
diseases, and therapeutic prospects.

AUTHOR(S): Battegay, E. J.

CORPORATE SOURCE: Dep. Res. Internal Med., University Hospitals,  
CH-4031

Basel Switzerland

SOURCE: Journal of Molecular Medicine (Berlin), (1995) Vol. 73,  
No.

7, pp. 333-346.

ISSN: 0946-2716.

DOCUMENT TYPE: General Review

LANGUAGE: English

AB This review of \*\*\*angiogenesis\*\*\* aims to describe (a) stimuli that  
either elicit or antagonize \*\*\*angiogenesis\*\*\*, (b) the response of  
the vasculature to \*\*\*angiogenic\*\*\* or anti- \*\*\*angiogenic\*\*\*  
stimuli, i.e., processes required for the formation of new vessels, (c)  
aspects of \*\*\*angiogenesis\*\*\* relating to tissue remodeling and  
disease, and (d) the potential of \*\*\*angiogenic\*\*\* or antiangiogenic  
therapeutic measures. \*\*\*Angiogenesis\*\*\*, the formation of new  
vessels

from existing microvessels, is important in embryogenesis, wound healing,  
diabetic retinopathy, tumor growth, and other diseases. Hypoxia and other  
as yet ill-defined stimuli drive tumor, inflammatory, and connective  
tissue cells to generate \*\*\*angiogenic\*\*\* molecules such as vascular  
endothelial growth factor (VEGF), fibroblast growth factor (FGF),  
transforming growth factor-beta (TGF-beta), platelet-derived growth  
factor

(PDGF), and others. Natural and synthetic angiogenesis \*\*\*inhibitors\*\*\*  
such as \*\*\*angiostatin\*\*\* and thalidomide can repress  
\*\*\*angiogenesis\*\*\*. \*\*\*Angiogenic\*\*\* and antiangiogenic  
molecules

control the formation of new vessels via different mechanisms. VEGF and  
FGF elicit their effects mainly via direct action on relevant endothelial  
cells. TGF-beta and PDGF can attract inflammatory or connective tissue  
cells which in turn control \*\*\*angiogenesis\*\*\*. Additionally, PDGF

may  
act differently on specific phenotypes of endothelial cells that are  
engaged in \*\*\*angiogenesis\*\*\* or that are of microvascular origin.  
Thus phenotypic traits of endothelial cells committed to

09/676 301  
Att #14

=> s angiogenesis(w)inhibitor  
L1 4497 ANGIOGENESIS(W) INHIBITOR

=> s angiostatin  
L2 1746 ANGIOSTATIN

=> s l1 and l2  
L3 502 L1 AND L2

=> s immunophilin or cyclophilin or (steroid(3n)receptor)  
L4 26808 IMMUNOPHILIN OR CYCLOPHILIN OR (STEROID(3N) RECEPTOR)

=> s l1 and l2 and l4  
L5 0 L1 AND L2 AND L4

=> s steroid receptor  
L6 12961 STEROID RECEPTOR

=> s steroid(3n)receptor  
L7 20221 STEROID(3N) RECEPTOR

=> s immunophilin  
L8 2202 IMMUNOPHILIN

=> s cyclophilin  
L9 5088 CYCLOPHILIN

=> s l7 or l8 or l9  
L10 26808 L7 OR L8 OR L9

=> s l1 and l10  
L11 10 L1 AND L10

=> dup rem l11  
PROCESSING COMPLETED FOR L11  
L12 9 DUP REM L11 (1 DUPLICATE REMOVED)

=> d l12 ibib abs 1-9

L12 ANSWER 1 OF 9 WPIDS (C) 2002 THOMSON DERWENT  
ACCESSION NUMBER: 2002-282788 [33] WPIDS  
CROSS REFERENCE: 2000-475722 [39]; 2000-491087 [42];  
2000-491116 [42]; 2000-491166 [42]; 2000-572155 [50]; 2001-016296 [66]  
DOC. NO. NON-CPI: N2002-220901  
DOC. NO. CPI: C2002-083226  
TITLE: Identifying patient having breast cancer or breast  
precancer, by examining ductal fluid sample from one duct  
of breast of patient to determine presence of marker such  
as protein, peptide, polypeptide, polynucleotide.  
DERWENT CLASS: B04 D16 P31 S03  
INVENTOR(S): HUNG, D  
PATENT ASSIGNEE(S): (PROD-N) PRO DUCT HEALTH INC  
COUNTRY COUNT: 29  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1182459	A2	20020227 (200233)*	EN	30	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV					
MC MK NL PT					
RO SE SI TR					
AU 2001057679 A		20020131 (200233)			
CA 2353193	A1	20020126 (200233)	EN		
JP 2002131322 A		20020509 (200234)		29	

#### APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1182459	A2	EP 2001-306350	20010724
AU 2001057679 A		AU 2001-57679	20010726
CA 2353193	A1	CA 2001-2353193	20010725
JP 2002131322 A		JP 2001-226849	20010726

PRIORITY APPLN. INFO: US 2000-625399 20000726  
AN 2002-282788 [33] WPIDS  
CR 2000-475722 [39]; 2000-491087 [42]; 2000-491116 [42]; 2000-491166 [42];

2000-572155 [50]; 2001-016296 [66]

AB EP 1182459 A UPAB: 20020528

NOVELTY - Identifying (M) a patient having breast cancer or breast precancer, involves providing a ductal fluid sample from one duct of a breast of a patient, where the fluid is not mixed with ductal fluid from any other duct of the breast, and examining the ductal fluid sample to determine the presence of a marker (I) that can be identified in the ductal fluid retrieved from the breast.

DETAILED DESCRIPTION - Identifying (M) a patient having breast cancer

or breast precancer, involves providing a ductal fluid sample from one duct of a breast of a patient, where the fluid is not mixed with ductal fluid from any other duct of the breast, and examining the ductal fluid sample to determine the presence of a marker (I) that can be identified in the ductal fluid retrieved from the breast.

In (M), (I) is selected from protein, polypeptide, peptide, nucleic acid, polynucleotide, mRNA, small organic molecule, lipid, fat, glycoprotein, glycopeptide, carbohydrate, oligosaccharide, chromosomal abnormality, whole cell having a marker molecule, particle, secreted molecule, intracellular molecule, and complex of number of molecules.

An INDEPENDENT CLAIM is also included for a system (II) for diagnosing breast cancer or precancer comprising a tool to retrieve ductal fluid from a breast duct and instructions for use to determine the presence of a marker identified in (M).

USE - (M) is useful for identifying a patient having breast cancer or breast precancer (claimed).

Dwg.0/0

L12 ANSWER 2 OF 9 EMBASE COPYRIGHT 2002 ELSEVIER SCI.  
B.V.

ACCESSION NUMBER: 2002248018 EMBASE

TITLE: Understanding mouse skin carcinogenesis through transgenic approaches.

AUTHOR: Larcher F.; Ramirez A.; Casanova M.L.; Navarro M.; Paramio

J.M.; Perez P.; Page A.; Santos M.; Jorcano J.L.

CORPORATE SOURCE: J.L. Jorcano, Proj. Cell/Mol. Biol./Gene Therapy, CIEMAT,

Av. Complutense 22, 28040 Madrid, Spain.

jl.jorcano@ciemat.es

SOURCE: Current Genomics, (2002) 3/4 (335-353).

Refs: 196

ISSN: 1389-2029 CODEN: CGUEA8

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 005 General Pathology and Pathological Anatomy

013 Dermatology and Venereology

016 Cancer

022 Human Genetics

037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The epidermis is a model particularly well suited to the study of cell proliferation and differentiation, and of alterations of these processes such as carcinogenesis. Compartmentalization exists in this tissue, with the proliferative, less differentiated cells confined to the basal layer and the terminally differentiating, non-proliferative cells moving upwards to the surface through distinct layers. Different genes are expressed throughout this process in a stage-of-differentiation-specific manner, and their promoters have been very useful in directing precise gene expression in transgenic mice. Other attractive characteristics of the epidermis include its external localization, which facilitates manipulation and observation, the possibility of obtaining primary keratinocytes that can be easily cultured and manipulated in vitro, and the existence of well-established protocols for chemical and UV carcinogenesis. The latter are invaluable tools for assessing the in vivo functions of the genes targeted in transgenic mice. These characteristics have made the epidermis a widely used model system in recent years for the study of molecular mechanisms of carcinogenesis. A wealth of transgenic mice generated

using epidermal-specific promoters, as well as knockout animals, have been used

to examine the role of genes involved in processes such as cell cycle control, cell signaling, cell growth and differentiation, and angiogenesis

SOURCE: Current Problems in Dermatology, (2000) 12/2 (45-50).  
 Refs: 8  
 ISSN: 1040-0486 CODEN: APDEBX  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 013 Dermatology and Venereology  
 037 Drug Literature Index  
 LANGUAGE: English

L14 ANSWER 2 OF 2 EMBASE COPYRIGHT 2002 ELSEVIER SCI.  
 B.V.  
 ACCESSION NUMBER: 2001106823 EMBASE  
 TITLE: Late-breaking breast cancer research: From genomics to new  
 drugs.  
 AUTHOR: Johnston S.R.D.  
 SOURCE: Breast Cancer Research, (1999) 1/1 (54-55).  
 ISSN: 1465-5411 CODEN: BCRRCT  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 005 General Pathology and Pathological Anatomy  
 016 Cancer  
 022 Human Genetics  
 030 Pharmacology  
 037 Drug Literature Index  
 LANGUAGE: English

<-----User Break----->

u  
 SEARCH ENDED BY USER  
 SEARCH ENDED BY USER

=> s expression(5n)control????  
 '?' TRUNCATION SYMBOL NOT VALID WITHIN 'CONTROL????'  
 '?' TRUNCATION SYMBOL NOT VALID WITHIN 'CONTROL????'  
 '?' TRUNCATION SYMBOL NOT VALID WITHIN 'CONTROL????'  
 '?' TRUNCATION SYMBOL NOT VALID WITHIN 'CONTROL????'  
 '?' TRUNCATION SYMBOL NOT VALID WITHIN 'CONTROL????'  
 The truncation symbol ? may be used only at the end of a search  
 term. To specify a variable character within a word use '!', e.g.,  
 'wom!n' to search for both 'woman' and 'women'. Enter "HELP  
 TRUNCATION" at an arrow prompt (=>) for more information.

=> help truncation  
 Truncation symbols are used to retrieve various forms of your search  
 terms. The symbols can be combined in one search term.

Symbol	Definition	Example	Retrieves
?	Any number of characters	S STEROID?	STEROID STERIODS STEROIDAL
	Left truncation in some fields	S ?METHANE TRIHALOMETHANE NITROMETHANE	
#	One or zero characters at the end of a term	S VAPOR#	VAPOR VAPORS
!	One character at the end of or within a term	S WOM!N	WOMAN WOMEN
!#	At least one character, and no more than two, at the end of a term	S STEROID!#	STERIODS STEROIDAL

Multiple occurrences of the '#' and the '!' are allowed.

Left truncation, using the three truncation types, is also available for some fields in certain files. Left truncation of a search term can be used alone or, in some cases, in combination with right truncation. The cases which may not be used are: '?text#', '#text?' and '!text?'. To learn whether any fields in the current file have left truncation, enter HELP SFIELDS at an arrow prompt (=>) in the file.

=> s expression(5n)control?  
 4 FILES SEARCHED...  
 L15 77983 EXPRESSION(5N) CONTROL?

=> s l1 and l15  
 L16 22 L1 AND L15

=> dup rem l16  
 PROCESSING COMPLETED FOR L16  
 L17 22 DUP REM L16 (0 DUPLICATES REMOVED)

=> d l17 ibib abs 1-22

L17 ANSWER 1 OF 22 WPIDS (C) 2002 THOMSON DERWENT  
 ACCESSION NUMBER: 2002-471244 [50] WPIDS  
 DOC. NO. CPI: C2002-133934  
 TITLE: Novel recombinant virus comprising hypoxia responsive  
 element that \*\*\*controls\*\*\* \*\*\*expression\*\*\* of  
 genes which modulate the replication of viruses, useful  
 for treating cancer.  
 DERWENT CLASS: B04 D16  
 INVENTOR(S): NICHOLSON, A C; POST, D E; VAN MEIR, E  
 PATENT ASSIGNEE(S): (UYEM-N) UNIV EMORY  
 COUNTRY COUNT: 97  
 PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2002026192 A2 20020404 (200250)\* EN 59  
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE  
 LS LU MC MW MZ  
 NL OA PT SD SE SL SZ TR TZ UG ZW  
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN  
 CO CR CU CZ DE DK  
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP  
 KE KG KP KR  
 KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ  
 NO NZ PH PL PT RO  
 RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU  
 ZA ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002026192 A2		WO 2001-US30236	20010926

PRIORITY APPLN. INFO: US 2000-235283P 20000926  
 AN 2002-471244 [50] WPIDS  
 AB WO 200226192 A UPAB: 20020807  
 NOVELTY - A recombinant virus (I) comprising a hypoxia and/or  
 Hypoxia-Inducible Factor (HIF) responsive element which  
 \*\*\*controls\*\*\*  
 the \*\*\*expression\*\*\* of a gene which modulates replication of virus  
 that cytolyses hypoxic tissues and cells, or cells and tissues containing  
 an active HIF pathway, where (I) cytolyses tumor cells in an hypoxia  
 dependent manner, is new.  
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also  
 included for the  
 following:  
 (1) a vector (II) comprising at least one hypoxia responsive element  
 operably linked to a reporter gene;  
 (2) a mammalian tumor cell line (III) containing a vector comprising  
 at least one hypoxia or HIF responsive element operably linked to a  
 reporter gene; and  
 (3) a compound (IV) detected using (III), where (IV) inhibits more  
 than 50% of the expression of the reporter gene, or has an IC50 less than  
 100 micro M for inhibiting the hypoxia inducible pathway.  
 ACTIVITY - Cytostatic, antiarthritic, antidiabetic, ophthalmological;  
 cerebroprotective; gynecological; vasotropic.  
 LN229 glioma cells was implanted subcutaneously into the left flank  
 of nu/nu mice. When the average tumor volume reached 75 mm3 the mice  
 was  
 divided into three groups and 0.66 multiply 108 pfu of adenovirus  
 (HYPR-Ad1 or d1309) or phosphate buffered saline (PBS) (vehicle) was  
 injected daily for five days. Forty-nine days following the injection, the  
 mice were sacrificed and the tumors were harvested. At the time of

formats for controlling, modulating and tuning recombination rates.  
 ADVANTAGE - The methods facilitate and improve recombination and add levels of control. Divergent nucleic acids can be shuffled to provide modulation and tuning of shuffling rates.  
 DESCRIPTION OF DRAWING(S) - The figure shows the schematic trans-splicing library strategy.  
 Dwg.4/5

L12 ANSWER 7 OF 9 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
 ACCESSION NUMBER: 2001106895 EMBASE  
 TITLE: 91st annual meeting of the American association for cancer research.  
 AUTHOR: Speirs V.; Schmeichel K.L.  
 CORPORATE SOURCE: V. Speirs, Molecular Medicine Unit, University of Leeds, St James University Hospital, Leeds LS9 7TF, United Kingdom  
 SOURCE: Breast Cancer Research, (2000) 2/4 (302-306).  
 ISSN: 1465-5411 CODEN: BCRRCT  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 016 Cancer  
 037 Drug Literature Index  
 LANGUAGE: English

L12 ANSWER 8 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1  
 ACCESSION NUMBER: 2000:41003 BIOSIS  
 DOCUMENT NUMBER: PREV200000041003  
 TITLE: Selective inhibition of amino-terminal methionine processing by TNP-470 and ovalicin in endothelial cells.  
 AUTHOR(S): Turk, Benjamin E.; Griffith, Eric C.; Wolf, Susan; Biemann, Klaus; Chang, Yie-Hwa; Liu, Jun O. (1)  
 CORPORATE SOURCE: (1) Center for Cancer Research, Massachusetts Institute of Technology, Cambridge, MA, 02139 USA  
 SOURCE: Chemistry & Biology (London), (Nov., 1999) Vol. 6, No. 11, pp. 823-833.  
 ISSN: 1074-5521.  
 DOCUMENT TYPE: Article  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 AB Background: The angiogenesis inhibitors TNP-470 and ovalicin potentially suppress endothelial cell growth. Both drugs also specifically inhibit methionine aminopeptidase 2 (MetAP2) in vitro. Inhibition of MetAP2 and changes in initiator methionine removal in drug-treated endothelial cells have not been demonstrated, however. Results: Concentrations of TNP-470 sufficient to inactivate MetAP2 in intact endothelial cells were comparable to those that inhibited cell proliferation, suggesting that MetAP2 inhibition by TNP-470 underlies the ability of the drug to inhibit cell growth. Both drug-sensitive and drug-insensitive cell lines express MetAP1 and MetAP2, indicating that drug sensitivity in mammalian cells is not simply due to the absence of compensating MetAP activity. With a single exception, detectable protein N-myristoylation is unaffected in sensitive endothelial cells treated with TNP-470, so MetAP1 activity can generally compensate when MetAP2 is inactive. Analysis of total protein extracts from cells pulse-labeled with (35S)-methionine following TNP-470 treatment revealed changes in the migration of several newly synthesized proteins. Two of these proteins were identified as glyceraldehyde-3-phosphate dehydrogenase (GAPDH) and \*\*\*cyclophilin\*\*\*  
 A. Purification and amino-terminal sequencing of GAPDH from TNP-470-treated cells revealed partial retention of its initiator methionine, indicating that methionine removal from some, but not all, proteins is affected by MetAP2 inactivation. Conclusions: Amino-terminal processing defects occur in cells treated with TNP-470, indicating that inhibition of MetAP2 by the drug occurs in intact cells. This work renders plausible a mechanism for growth inhibition by TNP-470 as a consequence of initiator methionine retention, leading to the inactivation of as yet unidentified proteins essential for endothelial cell growth.

L12 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:581686 HCAPLUS  
 DOCUMENT NUMBER: 131:317944  
 TITLE: Anti-angiogenic activity of a novel synthetic agent, 9.alpha.-fluoromethoxyprogesterone acetate  
 AUTHOR(S): Yamaji, T.; Tsuboi, H.; Murata, N.; Uchida, M.; Kohno, T.; Sugino, E.; Hibino, S.; Shimamura, M.; Oikawa, T.  
 CORPORATE SOURCE: Institute of Health Science, Meiji Milk Products Co., Ltd., Kanagawa, Japan  
 SOURCE: Cancer Letters (Shannon, Ireland) (1999), 145(1,2), 107-114  
 CODEN: CALEDQ; ISSN: 0304-3835  
 PUBLISHER: Elsevier Science Ireland Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB 9.alpha.-Fluoromethoxyprogesterone acetate (FMPA) is a novel synthetic analog of medroxyprogesterone acetate (MPA), widely used as therapeutic agent for breast and endometrium cancers. FMPA showed almost the same binding affinities to the progesterone and glucocorticoid receptors as MPA. In the rabbit corneal assay, FMPA, MPA and fumagillin significantly inhibited the angiogenic response induced by rat mammary tumor at doses of 0.1, 1 and 50 .mu.g/pellet, resp., so FMPA showed greater anti-angiogenic activity than MPA and fumagillin. In the mouse dorsal air sac method, FMPA inhibited the mouse sarcoma 180 cell-induced angiogenesis by oral administration at a dose of 200 mg/kg. FMPA inhibited the activity of plasminogen activator (PA) in bovine endothelial cells. These results suggest that FMPA may be useful for diseases assocd. with angiogenesis by oral administration.  
 REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

=> d his

(FILE 'HOME' ENTERED AT 17:52:21 ON 07 AUG 2002)

FILE 'BIOSIS, EMBASE, MEDLINE, WPIDS, HCAPLUS' ENTERED AT 17:52:32 ON 07 AUG 2002

L1 4497 S ANGIOGENESIS(W)INHIBITOR  
 L2 1746 S ANGIOSTATIN  
 L3 502 S L1 AND L2  
 L4 26808 S IMMUNOPHILIN OR CYCLOPHILIN OR (STEROID(3N)RECEPTOR)  
 L5 0 S L1 AND L2 AND L4  
 L6 12961 S STEROID RECEPTOR  
 L7 20221 S STEROID(3N)RECEPTOR  
 L8 2202 S IMMUNOPHILIN  
 L9 5088 S CYCLOPHILIN  
 L10 26808 S L7 OR L8 OR L9  
 L11 10 S L1 AND L10  
 L12 9 DUP REM L11 (1 DUPLICATE REMOVED)

=> s l2 and l10

L13 2 L2 AND L10

=> dup rem l13

PROCESSING COMPLETED FOR L13

L14 2 DUP REM L13 (0 DUPLICATES REMOVED)

=> d l14 ibib abs 1-2

L14 ANSWER 1 OF 2 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
 ACCESSION NUMBER: 2000173437 EMBASE  
 TITLE: Psoriasis: A view for the year 2000.  
 AUTHOR: Ellis C.N.; Barker J.N.W.N.  
 CORPORATE SOURCE: Dr. C.N. Ellis, Department of Dermatology, University of Michigan, Ann Arbor, MI, United States

that  
of \*\*\*controls\*\*\*. The decrease in VEGF expression in SW620 cells  
was  
dose dependent, with a 49% decrease obsd. at a multiplicity of infection  
of 50, and a 71% decrease obsd. at a multiplicity of infection of 100.  
Similar effects were seen in KM12L4 cells. VEGF supernatant protein  
levels were significantly reduced compared with those in nontransduced  
controls 48 h after the introduction of wild-type p53. Ad5/CMV/p53  
inhibited tumor cell-induced angiogenesis in vivo. Restoration of  
wild-type p53 expression may decrease tumor growth by inhibiting the  
angiogenic response. These findings may explain, in part, the bystander  
effect seen with p53 tumor suppressor gene therapy.

=> d his

(FILE 'HOME' ENTERED AT 17:52:21 ON 07 AUG 2002)

FILE 'BIOSIS, EMBASE, MEDLINE, WPIDS, HCAPLUS' ENTERED  
AT 17:52:32 ON 07  
AUG 2002

L1 4497 S ANGIOGENESIS(W)INHIBITOR  
L2 1746 S ANGIOSTATIN  
L3 502 S L1 AND L2  
L4 26808 S IMMUNOPHILIN OR CYCLOPHILIN OR  
(STEROID(3N)RECEPTOR)  
L5 0 S L1 AND L2 AND L4  
L6 12961 S STEROID RECEPTOR  
L7 20221 S STEROID(3N)RECEPTOR  
L8 2202 S IMMUNOPHILIN  
L9 5088 S CYCLOPHILIN  
L10 26808 S L7 OR L8 OR L9  
L11 10 S L1 AND L10  
L12 9 DUP REM L11 (1 DUPLICATE REMOVED)  
L13 2 S L2 AND L10  
L14 2 DUP REM L13 (0 DUPLICATES REMOVED)  
L15 77983 S EXPRESSION(5N)CONTROL?  
L16 22 S L1 AND L15  
L17 22 DUP REM L16 (0 DUPLICATES REMOVED)

=> s angiogenesis or angiogenic or angiostatin

L18 71510 ANGIOGENESIS OR ANGIOGENIC OR ANGIOSTATIN

=> s l15 and l18

L19 891 L15 AND L18

=> s inhibit?

L20 4584123 INHIBIT?

=> s l15 and l18 and l20

L21 346 L15 AND L18 AND L20

=> dup rem l21

PROCESSING COMPLETED FOR L21

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=> s l22 and py<1998

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L23 27 L22 AND PY<1998

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L23 ANSWER 1 OF 27 BIOSIS COPYRIGHT 2002 BIOLOGICAL  
ABSTRACTS INC.

ACCESSION NUMBER: 1997:403280 BIOSIS

DOCUMENT NUMBER: PREV199799709483

TITLE: The paracrine role of tumour-derived mIL-4 on  
tumour-associated endothelium.

AUTHOR(S): Saleh, Mary (1); Davis, Ian D.; Wilks, Andrew F.

CORPORATE SOURCE: (1) Dep. Surgery Neurosurgery, University  
Melbourne,  
Clinical Sci. Build., Level 5, Grattan St., Parkville, VIC  
3050 Australia

SOURCE: International Journal of Cancer, (1997) Vol. 72, No. 4, pp.  
664-672.  
ISSN: 0020-7136.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Interleukin-4 (IL-4) has been demonstrated to possess anti-tumorigenic  
properties in vivo which is initially attributed to the infiltration of  
eosinophils proposed to occur by IL-4 binding to its receptors on  
endothelial cells, thereby mediating eosinophil adhesion. We have  
investigated whether the binding of IL-4 to receptors on endothelial cells  
could elicit other biological responses which may also play a role in  
tumour \*\*\*inhibition\*\*\*, such as \*\*\*angiogenesis\*\*\*. We have  
demonstrated that mouse IL-4 (mIL-4) down-regulates the expression of  
one

of the receptors for VEGF, VEGF-R2, on endothelial cells in vitro. By  
generating stable transfectants of C6 glioma cells that express mIL-4  
under a tetracycline-responsive promoter system, we were able to apply  
tight regulatory \*\*\*control\*\*\* of mIL-4 \*\*\*expression\*\*\* in vivo.  
Subcutaneous implantation of mIL-4/C6 cell lines in nu/nu mice revealed  
that tumour growth is \*\*\*inhibited\*\*\* by mIL-4 expression.  
mIL-4-expressing tumours were demonstrated to have a reduced level of  
vascularization compared with controls, in addition to a high degree of  
eosinophil infiltration. Our results suggest that mIL-4 has bimodal  
biological roles in potentiating tumour \*\*\*inhibition\*\*\* in athymic  
mice: the suppression of \*\*\*angiogenesis\*\*\* and the augmentation of  
the host local immune response.

L23 ANSWER 2 OF 27 BIOSIS COPYRIGHT 2002 BIOLOGICAL  
ABSTRACTS INC.

ACCESSION NUMBER: 1997:367310 BIOSIS

DOCUMENT NUMBER: PREV199799659243

TITLE: The matrix metalloproteinase RASI-1 is expressed in  
synovial blood vessels of a rheumatoid arthritis patient.

AUTHOR(S): Kolb, Cornelia; Mauch, Simon; Peter, Hans-Hartmut;  
Krawinkel, Ulrich; Sedlacek, Radislav (1)

CORPORATE SOURCE: (1) Fac. Biol., Univ. Konstanz, P.O. Box  
5560M661, D-78464

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SOURCE: Immunology Letters, (1997) Vol. 57, No. 1-3, pp. 83-88.

ISSN: 0165-2478.

DOCUMENT TYPE: Article

LANGUAGE: English

AB RASI-1 is a novel matrix metalloproteinase which we isolated from an  
expression cDNA library representing the mRNA of an inflamed synovium  
obtained from a patient with rheumatoid arthritis (RA). To investigate the  
involvement of RASI-1 in the pathology of RA, we examined synovial  
specimens from RA patients with antibodies directed against an unique  
RASI-1-derived peptide. In comparison to interstitial collagenase,  
gelatinase A and B, and stromelysin 1, the RASI-1 expression in the  
RA-synovium is located mainly in the tunica media of blood vessel walls  
and its synovial localization is not as ubiquitous as that of other MMPs.  
The tissue \*\*\*inhibitor\*\*\* of metalloproteinases (TIMP-1), although  
also widely expressed in the synovium, exhibits strong colocalization with  
RASI-1 in blood vessel walls. While RASI-1 is expressed in blood vessels  
of the inflamed synovium of an RA patient, its \*\*\*expression\*\*\* was  
not found in \*\*\*control\*\*\* synovial specimens from patients with  
luxation and arthrosis. However, RASI-1 expression can also be found in  
non-inflamed blood vessels of uterine ligaments and skin. RASI-1,  
although

its function and substrates are unknown, could be involved in processes  
such as neovascularization and \*\*\*angiogenesis\*\*\* or lymphocyte  
extravasation and thus may participate in joint tissue destruction during  
RA.

L23 ANSWER 3 OF 27 BIOSIS COPYRIGHT 2002 BIOLOGICAL  
ABSTRACTS INC.

ACCESSION NUMBER: 1997:363269 BIOSIS

DOCUMENT NUMBER: PREV199799655202

TITLE: Stretch-induced VEGF expression in the heart.

AUTHOR(S): Li, Jian; Hampton, Thomas; Morgan, James P.; Simons,  
Michael (1)

CORPORATE SOURCE: (1) Cardiovascular Div., Beth Israel Hosp., R453,  
330

Brookline Avenue, Boston, MA 02215 USA

SOURCE: Journal of Clinical Investigation, (1997) Vol. 100, No. 1,  
pp. 18-24.

ISSN: 0021-9738.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Vascular endothelial growth factor (VEGF) is an endothelial cell  
mitogen